The Journal OF THE South Carolina Medical Association

VOL. XVI. GREENVILLE, S. C., FEBRUARY, 1920 NO. 2

Dr. O. M. Wood

CONTENTS

EDITORIAL DEPT.:

An Article with X-Ray Plates on Oesophageal Diverticula 27

The Provisional Program for Greenville Meeting 28

Columbia Society Progressive..... 29

The Schick Test and Toxin-Antitoxin Immunization Approved by State Board of Health..... 30

Plans for the Greenville Meeting Nearing Completion 30

Post Graduate Instruction for County Societies 30

Death of Dr. T. A. Crawford..... 31

Council Passed 31

Foreword in Reference to Article on Anaphylaxis and Anti-Anaphylaxis 31

ORIGINAL ARTICLES:

Anaphylaxis and Anti-Anaphylaxis by C. V. Akin, Columbia, S. C.... 32

Annual Report of the State Health Officer 50

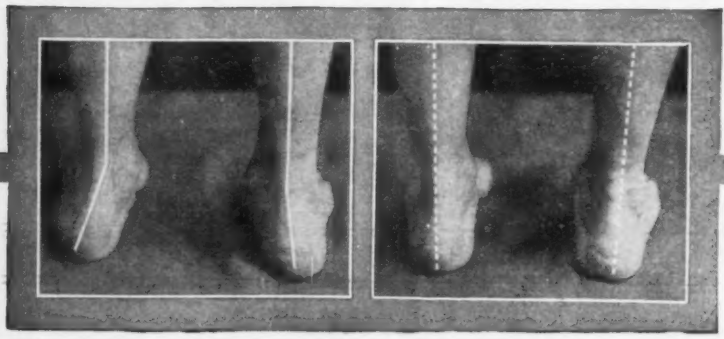
BOOK REVIEWS 51

The Baker Sanatorium

Colonial Lake **Charleston, S. C.**

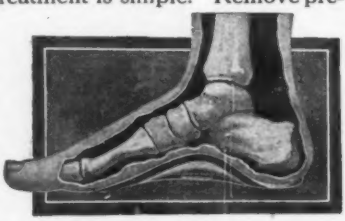
ARCHIBALD E. BAKER, M. D., F. A. C. S. Surgeon in Charge.

A New and thoroughly equipped hospital for the care of Surgical patients.



Weak Arch and Flat-foot—

that need mechanical correction are very prevalent and frequently are associated with painful heel, callouses on sole, fatigue, nervousness, neurasthenia, physical exhaustion and rheumatic tendencies. Heavy people and those who are constantly on their feet, and whose occupation requires them to assume a posture conducive to the weakening of the leg and foot muscles, are usually victims of these complaints. The corrective treatment is simple. Remove predisposing causes such as short hosiery, improperly fitted or constructed shoes, and have patient fitted to



Dr Scholl's
Corrective Foot Appliances

which are scientifically constructed to relieve muscular and ligamentous strain, remove abnormal pressure and restore feet to usefulness. There are distinct types of appliances for each condition. All quickly and easily adjusted to any degree of elevation or curvature, assuring the physician dependable results.

Leading shoe dealers and surgical supply houses in every locality carry Dr. Scholl's Appliances and have also been instructed in Anatomy of the Foot and the proper method of adjusting the appliances to fit both foot and shoe.

Send Coupon for New Pamphlet

Dr. _____

Street _____

City _____ *State* _____

Fill out the coupon for your copy of "Foot Weakness and Correction for the Physician"—just published.

Write for important pamphlet just published, "Foot Weakness and Correction for the Physician," and a chart of Foot exercises as endorsed by the United States Army Medical Dept.

The Scholl Mfg. Co.
213 W. Schiller Street
Chicago

New York Toronto London, Eng.

The Journal OF THE South Carolina Medical Association

Published Every Month Under the Direction of the Board of Councilors.

Entered as second-class matter February 9, 1916, at the post office at Greenville, South Carolina, under the Act of March 3, 1879.
Acceptance for mailing at special rate of postage provided for in Sec. 1103 Act of October 3, 1917, authorized August 2, 1918.

Annual Subscription, $2.00. EDGAR A. HINES, M. D., Editor-in-Chief, Seneca, S. C.

ASSOCIATE EDITORS.

INTERNAL MEDICINE.
J. H. GIBBES, M. D., Columbia, S. C.

PEDRIATICS.
WM. WESTON, M. D., Columbia, S. C.
R. M. POLLITZER, M. D., Charleston, S. C.
D. L. SMITH, M. D., Spartanburg, S. C.

OBSTETRICS.
G. FRASER WILSON, M. D., Charleston, S. C. Department of Obstetrics, Medical College State of South Carolina.

GENITO-URINARY DISEASES AND SEROLOGY.
M. H. WYMAN, M. D., Columbia, S. C.

SURGERY.
G. T. TYLER, M. D., Greenville, S. C.
R. LEE SANDERS, Memphis, Tenn.

UBLIC HEALTH.
C. V. AKIN, M. D., U. S. P. H. Columbia, S. C., Assistant Sec. State Board of Health.
ERNEST COOPER, M. D., Columbia, S. C., South Carolina Sanatorium.
MRS. RUTH A. DODD, R. N., Columbia, S. C., Bureau of Child Hygiene.
C. F. WILLIAMS, M. D., Columbia, S. C.
J. F. MUNNERLYN, M. D., Columbia, S. C., South Carolina Hospital for the Insane.
A. E. BOOZER, M. D., Columbia, S. C., State Board fo Medical Examiners.
A. ROBERT TAFT, M. D., Charleston, S. C., Department of Roentgenology, Medical College.
KENNETH M. LYNCH, M. D., Charleston, S. C., Department of Pathology, Medical College.

EYE, EAR, NOSE, AND THROAT.
E. W. CARPENTER, M. D., Greenville, S. C.

EDITORIAL

AN ARTICLE WITH X-RAY PLATES ON OESOPHAGEAL DIVERTICULA.

The 1919 Collected Papers of the Mayo Clinic contains many articles of interest pertaining to X-ray diagnosis and Radium Therapy.

An article by Dr. Carman, Chief of the Section of Roentgenology, deals with the Radiologic Aspects of Hourglass stomachs. Ulcer, cancer, syphilis, tuberculosis and perigastric inflammation and the differentiation of the same. He calls our attention to the spasm as simulitating these conditions. The possibility of relaxing this with Antispasmodies and that the spasm as seen by the Roentgenologist is not seen by the surgeon because it disappears with narcosis. A case of Polyposis of the stomach is discussed by Dr. Balfour, with full credit to the X-ray for diagnosis of the same. Syphilis of the stomach with report of 40 cases, by Dr. Eusterman is an article of much interest. He included some instructive plates and Dr. Carman's deductions concerning the characteristic points in Radiological diagnosis of this condition. In a review of 117 cases of Chronic Ulcerative Colitis by Dr. Logan, the X-ray findings are stated, and many plates included in the

article. An article by Dr. Judd on Carcinoma of the small intestine, the X-ray findings are shown. The chapter on Uro-genital Organs contains articles by Drs. Judd and Harrington on Ectopic kidney with X-ray plates of same. The Radiographic diagnosis in Renal Tuberculosis by Drs. Braasch and Olsen contains many interesting findings of this method of diagnosis. The extending from the kidneys to the Prostrate. Dr. Peterson in an article entitled the effect on the kidney of uretero-vesical anastomosis introduces Pyelograms as showing the final condition of the kidney pelvis. Prostatic Calculi, as discussed by Drs. Judd and Crenshaw, state X-ray diagnosis positive in 75 per cent of the series. Diverticula of the Bladder by Dr. Judd also gives full credit to the X-ray and shows many plates. Dr. Stokes in an article on Cutaneous aspects of Tuberculosis, concluded that X-ray treatment of the focus in a glandular case has its function but cannot displace Arsphenamin. A review of the Roentgenology of Syphilis, by Dr. Carman takes up syphilis in the bones, joints, Aorta, lungs, stomach, and Duodenum. An article by Dr. Meyerding on Cystic and Fibrocystic disease of the long bones contains many Roentgenograms of interest. Articles by Dr. New on The Value of Radium in Treatment of the Neoplasm of Nose, Throat and Mouth and Use of Heat and Radium in the Treatment of Cancer of the Jaws and Cheeks, would tend to show what an important place Radium has taken in the treatment of many conditions as an assistant to surgery. An article by Dr. Stacy considers the Treatment of Menorrhagia with Radium and emphasizes the fact that this remedy is very valuable in idiopathic hemorrhages and moderate size Fibroids and even large Fibroids where surgical risk is great. Dr. Griffin, in an article entitled Splenectomy following Radium treatment for Myelotic Leukemia, states that the Spleen and the Leucocyte count were much reduced by means of Radium and the general condition of the patient very much improved. Dr. Luden, in Studies on Cholesterol in Malignant disease and the effect of Radium on the blood cholesterol, concludes that Radium treatment by reducing the unchanged Cholesterol and increasing the changed Cholesterol, affects the chemical composition of the blood—a fact that has not been hitherto taken into account but which may play an important part in the beneficial effect of Radium therapy on these conditions.

A. ROBERT TAFT, M. D.
Department of Roentgenology, Medical College, Charleston, S. C.

THE PROVISIONAL PROGRAM FOR GREENVILLE MEETING.

The following papers have been promised for the Greenville meeting:

Annual address in surgery: Dr. Stuart McGuire, of Richmond, Va.

Annual address in internal medicine: Professor E. H. Goodman, University of Pennsylvania.

Dr. William R. Barron: "A New Treatment for Enuresis in Children," Columbia, S. C.

Dr. George Benet: "Carcinoma of the Male Breast." Columbia, S. C.

Dr. J. W. Babcock: "Medical Certificates of Insanity." Columbia, S. C.

Dr. W. F. Phillips: (Subject Unannounced). Medical College, Charleston, S. C.

Dr. F. M. Durham: "A Few Remarks on the Treatment of Chronic Dysentery." Columbia, S. C.

Dr. Kenneth M. Lynch: "Diagnostic Incision of Tumors," Medical College, Charleston, S. C.

Dr. John F. Townsend: "Resume of Some Foreign Body Cases." Charleston, S. C.

Dr. Lindsay Peters: "A Method of Inducing the Rapid Growth of Epithelium over Areas Denuded of Skin, by the use of Zinc Oxide Adhesive Plaster Applied Directly to the Raw Area." Columbia, S. C.

Dr. Samuel Orr Black: (Subject Unannounced). Spartanburg, S. C.

Dr. G. T. Tyler: (Subject Unannounced). Greenville, S. C.

Dr. P. V. Mikell: "Radical Peritonsillar Abscess." Columbia, S. C.

Dr. J. R. Young: "Hospital Standardization in South Carolina." Anderson, S. C.

COLUMBIA SOCIETY PROGRESSIVE.

In response to our request, the reports of the County Societies are now coming in, and are full of interest. We are glad to present herewith, the report of the last meeting of the Columbia Medical Society. We look forward to reports regularly now, from all of our societies, and this is no small matter, because The Journal not only reaches more doctors in South Carolina than any other journal, but it has a large exchange list throughout the United States. It is our duty to let the world know what we are doing.

Columbia, S. C., Jan. 22, 1920.

The Editor Journal:

We would like to report the last meeting of the Columbia Medical Society, held in the hall in the Arcade Building. Papers were read on the followin gsubjects:

Institutional vs. Home Care of the Confinement Case.—Dr. Theo. M. DuBose, Jr.

Pyelitis Complicating Pregnancy.—Dr. Clarence F. Owens.

Some Helpful Details in Obstetrical Work.—Dr. Jane Bruce Gignard.

Nitrous Oxide in Obstetrics.—Dr. H. H. Griffin.

The discussion of these papers was very full. Drs. McIntosh, Siebels and Jennings were to lead, but the papers were so well prepared and so well presented that the whole society took a hand in the discussion.

The paper by Dr. Guignard caused quite a lot of comment as it was filled with meat from the opening paragraph to the final period.

Dr. DuBose brought down the storm by advocating hospital care of the confinement case, but in closing the discussion of his paper he brought his opponents up with a round turn when he stated that the average labor case could be conducted in a hospital for from thirty to fifty dollars with trained nurses and without the use of a "clean negro assistant?"

Dr. Owens' paper did not come in for the discussion that it merited, due to the fact that the Urologists were late in arriving.

Dr. Griffin's paper was excellent, and he contends that a mother can go through labor with safety and with a minimum of pain by using nitrous oxide.

The attendance was the best we have had for some time. The next meeting will be held at the State Hospital, and we expect it to be one of the best meetings of the year.

The Columbia Medical Society extends to every man in the state a hearty welcome to its meetings which are held on the second Monday of each month. You can depend on hearing good papers and a lively discussion.

GEORGE H. BUNCH,
FLOYD D. ROGERS, President.
Sec. & Treas.

THE SCHICK TEST AND TOXIN-ANTITOXIN IMMUNIZATION APPROVED BY STATE BOARD OF HEALTH.

At the meeting of the State Board of Health, December 30, 1919, the matter of furnishing the Schick Test and toxin-antitoxin for the use of the physicians of the State, was discussed and approved of; and at the time for giving out the contracts for 1920 it is highly probable that this valuable method of protecting the children of our State from the ravages of diphtheria will be furnished the profession free of charge as is now done with diphtheria anti-toxin. This is in line with the well-known progressive policy of the State Board of Health of South Carolina.

PLANS FOR THE GREENVILLE MEETING NEARING COMPLETION.

The President and Secretary of the South Carolina Medical Association, met with the committee on arrangements, representing the Greenville County Medical Society, on Friday evening, January 23rd, and perfected plans for the coming meeting of the State Medical Association in Greenville, April 20-21. The Association is most fortunate in having as its guests, Dr. Stuart McGuire, the eminent surgeon of Richmond, Va., and who is so well and favorably known throughout the entire South. Also, Professor E. H. Goodman, of the department of internal medicine, of the University of Pennsylvania, an internist of unquestioned ability, and a most interesting speaker. The Surgeon General of the Public Health Service will detail an expert to present the anti-venereal campaign. It is highly probable that, owing to the interest of Greenville in public health matters generally, the Association will put on a public health Sunday in the churches of the city, preceding the meeting of the Association. It is expected that at least three hundred physicians will attend the meeting in Greenville. The House of Delegates will convene at 10 a. m., Tuesday, April 20th, and will complete its business early in the afternoon. The evening will be given over to the address of Dr. McGuire and possibly the speaker representing the public health service, after which a reception will be tendered the President of the Association and an opportunity given to the citizens of Greenville to meet the members of the Association. The committee on arrangements appointed by the Greenville County Society, is as follows:

Dr. W. M. Burnett, chairman.
Dr. C. B. Earle.
Dr. R. E. Houston.
Dr. C. O. Bates, secretary.
Dr. E. W. Carpenter.

Any inquiry on the part of our members, with reference to accommodations may be addressed to the chairman of this committee ,though further details as to this matter will be given later.

POST GRADUATE INSTRUCTION FOR COUNTY SOCIETIES.

Details of the plan to put on post graduate instruction in certain sections of the State, which will include clinics as well as didactic lectures by teachers of unquestioned ability, are rapidly assuming shape to present to the State Medical Association at Greenville for the approval of the members. It is hoped that the plans will be so far advanced that immediately upon the close of the Association these courses may begin simultaneous-

ly in various parts of the State. The officers have conferred with the State Board of Health, the Medical College, the Extension Department of the University of South Carolina, and in each instance a promise of hearty co-operation has been secured.

DEATH OF DR. T. A. CRAWFORD.

The death of one of our oldest honorary members, occurred November 11th, at Rock Hill, S. C. Dr. Crawford was a physician of the old school ,a highly honored and useful citizen, and for more than a quarter of a century rendered conspicuous service as the resident trustee of Winthrop College. The following resolutions have been adopted by the brethren of the medical profession, with whom he was closely associated and who know him best.

Rock Hill, S. C., Jan. 3, 1920.

Whereas, the All-wise Providence has seen proper to remove from our midst by death, Dr. Thomas A. Crawford, and whereas, Dr. Crawford has been for years a member, both active and honorary, of the Rock Hill Medical Association, and whereas Dr. Crawford in his daily life and professional conduct exemplified many of the gentlemanly and humane virtues of our profession.

THEREFORE, BE IT RESOLVED:

First, That the Rock Hill Medical Association has sustained in the death of Dr. Crawford a very great loss, and the profession one of its best exponents.

Second, We hereby bear testimony to Dr. Crawford's many kindly traits, gentlemanly characteristics and noble ideals.

Third, We hereby extend to the family our most heartfelt sympathies and direct that a page in our minute books be inscribed to the memory of Dr. T. A. Crawford.

R. O. SUMNER, Pres.
W. FRANK STRAIT, Sec.

COUNCIL PASSED.

The attention of our readers is called to the "Council Passed" announcement of The Abbott Laboratories, on another page. We bespeak for this advertiser the support and patronage of our members. This firm is doing splendid research work, and the scientific products which it is developing include medicinal chemicals never before made in this country.

The research laboratories of several universities are co-operating with The Abbott Laboratories, to aid them in presenting to the medical profession original, scientific ideas in medicinal chemistry.

Judging from the growth of the Abbott Laboratories, this original, scientific work is being appreciated by the medical profession.

FOREWORD IN REFERENCE TO ARTICLE ON ANAPHYLAXIS AND ANTI-ANAPHYLAXIS

The following articles elsewhere in this issue is for the greater part merely a compilation of well authenticated data relating to the phenomena of ANAPHYLAXIS—in which the subject is rendered hypersensitive to the effects of unchanged protein, parenterally introduced—, and the beneficent condition of ANTI-ANAPHYLAXIS—in which the sensitized subject is naturally or deliberately desensitized or returned to the normal state.

Unless properly guarded against, the human recipient of horse serum, administered prophylactically or therapeutically in connection with diph-

theria, tetanus, cerebro-spinal meningitis, etc., is liable to most serious consequences instead of the almost magical benefits to be expected from specific serum therapy.

In view of the increasing widespread use of serum products by the general practitioners of medicine it behooves the physician to acquaint himself with the grave dangers of anaphylactic shock, and to be prepared to safeguard his patients against this unfortunate occurence.

No greater boon has been accorded mankind than the use of specific sera and antitoxins. The indiscriminate and careless misuse of these preparations will result in the production of public fear and distrust and consequently limit the service to which they can be applied.

In the application of specific serum therapy "luck" must play no part—success and safety are the rewards of painstaking scientific precaution.

The writer hopes that this simple collection of information may prove of interest and assistance to the medical profession of South Carolina to which it is respectfully presented.

C. V. AKIN.

513 Palmetto Building, Columbia, S. C., 1919.

ORIGINAL ARTICLES

ANAPHYLAXIS AND ANTI-ANAPHYLAXIS

C. V. Akin—Passed Assistant Surgeon, U. S. Public Health Service, Assistant State Health Officer for South Carolina. Columbia, S. C., 1919

A resume of the existing knowledge concerning the phenomena of sensitization and desensitization

THE earliest observations bearing directly upon the phenomenon of anaphylaxis, or hypersensibility to foreign protein when introduced unchanged into the animal body, were those reported by Magendie in 1839, in describing the sudden death of dogs which had been repeatedly injected with egg albumin. Flexner in 1894 made a clear statement of the fundamental phenomena and performed certain experiments in justification of his observations. These, and other isolated observations, proved to be of but temporary interest and no systematic study of the problem was made until Richet and Portier attacked it in 1902.

It was Charles Richet, (1) the French scientist, who coined the term "Anaphylaxis" to express the condition of increased susceptibility to poisons which followed a preliminary injection administered several days previously. Richet not only furnished the identifying name but actually created the subject itself for he showed anaphylaxis to be, not an isolated fact or accidental occurrence, but a phenomenon of widespread significance.

It is true that Richet and Portier, like V. Behring and others of his time, were working with primarily toxic substances, which, if administered in large enough doses, would have killed

Read before the Annual Meeting of the Pee Dee Medical Association, Florence, S. C., November 21, 1919.

but it is only fair to accord Richet the distinction of having laid the ground work for subsequent accomplishment in this section of biologic research.

In 1903 Arthus (2) reported his researches on the production of hypersensitiveness in rabbits by the repeated administration of horse serum. His observations were all the more significant because horse serum has no toxic properties for normal rabbits. Arthus noted that the first three injections of serum were reabsorbed without either local or systemic reactions but that the fourth injection resulted in local infiltration. A fifth injection, even though given into some other part of the body or into different tissue, caused the infiltrated areas to become markedly indurated. Continued injections caused these lesions to assume the appearance of gangrene. Arthus also caused death in animals which had received several subcutaneous injections by injecting the serum intravenously.

The "Phenomenon of Theobald Smith" as described by Otto (3) is closely related to that of Arthus and was observed in the course of the standardization of diphtheria antitoxin in guinea pigs. It was noted that such of these animals as survived the standardization procedure were promptly killed if subsequently injected with horse serum, days or even weeks later.

In 1906 Rosenau and Anderson (4) attacked the problem with the primary purpose of explaining certain deaths which had occurred following the injection of diphtheria antitoxin into human beings.

Working with guinea pigs and normal horse serum Rosenau and Anderson established certain fundamental facts which have remained aniomatic in the consideration of the anaphylactic reactions. These writers observed and proved conclusively, that a single minute injection of harmless serum served to sensitize, or render the animal hypersusceptible to subsequent injections of the same serum, provided a definite incubation period of from 10 to 12 days be permitted to elapse between the first and second injection. The specificity of the sensitization so produced was absolute, anaphylactic symptoms only occurring if the second injection was identical in substance with the first. They discovered that a normal animal could be rendered immediately sensitive without an incubation period by the injection of blood serum of an animal of the same or different species which had been previously sensitized, and that the young pigs born of sensitized mothers were hypersensitive to the same protein with which the mother had been sensitized. Further experiments showed also that sensitization could be carried out with various animal and vegetable proteins, various bacterial extracts serving to anaphylacticize as completely and specifically as the more concentrated horse serum. By these latter observations the possibility of a direct relation between anaphylaxis and bacterial infection was indicated.

Since the work done by Rosenau and Anderson, many investigators have been attracted to this new and facinating field. The bibliography of this subject is replete with the names of famous scientists, and libraries have been filled with reports of the researches undertaken to explain the mechanism of the production of these intense body reactions to the introduction of apparently harmless substances. Wonderful progress has been made since the first isolated observations called the attention of the scientific world to the fundamental phenomena

of sensitization. It is possible that our entire conception of the subjects of infection and immunity must be remodeled if the several well established hypotheses are accepted as fact.

In studies of this sort plausibility cannot be taken for proof. We are dealing with body substances and reactions infinitely too delicate to be seen or to be subjected to the relatively crude tests with which we are familiar. The entire structure of the research is based upon hypothesis, even the causative factors of the production of anaphylaxis are the subjects of conjectural reasoning.

It is neither desirable nor necessary to attempt to assign greater comparative importance to the studies of one observer than another. Present day knowledge of the subject of anaphylaxis was not arrived at by isolated single strokes of genius but is the result of exhaustive reasoning and unremitting toil on the part of a large number of great minds. As in other lines of development, certain researches stand out, either because of new ideas expressed or because the observer has been able to bring order out of the confusion of fact and theory resulting from the work of a number of investigators, each conducting research independent of the other.

Of the outstanding investigations along the line of protein hypersensitiveness those of Besredka and Steinhardt are certainly worthy of special consideration. In 1907 the work of Rosenau and Anderson and Otto covered the existing field of knowledge of the phenomenon of anaphylaxis.

The memoirs of Besredka and Steinhardt (5) published during 1907 presented both anaphylaxis and anti-anaphylaxis from the new angle of their own original research, and served to place the subject of anti-anaphylaxis upon a sound scientific basis. Since the presentation of his original monograph Besredka has been chiefly concerned with the study of anti-anaphylaxis and our thanks are due to him for developing a procedure of protective serum inoculations which will afford the maximum of safety to sensitized persons, who, because of the intercurrence of infection, must be subjected to further serum therapy.

Theories relating to the mechanism or causation of anaphylaxis are many and varied, all ingenious but not equally susceptible of proof. According to Charles Richet, the father of anaphylaxis, the condition is a true intoxication caused by a poison, apotoxin, resulting fro mthe combination in the body of a toxin-producing substance with the antigen (horse serum). Friedburger believes the toxic agent to be an anaphylotoxin. According to Friedburger the anaphylactic antibody is identical with the antibody "precipitin". At the time of the second injection the antibody combines with the antigen (horse serum) thereby forming a precipitate. This precipitate and the complement of the circulating blood combine to form anaphylotoxin, which in turn exerts its poisonous effect upon the body cells. Kraus and Biedl base their conception of anaphylaxis upon circulatory changes while Auer and Lewis look to the lungs for the explanation of death. According to Nicolle and Abt, the hypersensitiveness of guinea pigs is explained by the development of lysin, and anti-anaphylaxis results from the reduction of lytic power. Doerr formulated a "physical theory" in which the combination of horse serum and antibody in the blood results in certain modifications in the blood itself which produces the anaphylactic symptoms. Besredka and

others incline toward the physical rather than the anaphylotoxic theory.

The present day conception of anaphylaxis, as held by the average observer, is based either upon the protein-split poison theory of Vaughn and Wheeler or the purely physical conception of anaphylaxis as presented by Besredka in 1907. These diametrically opposed theories are both related so that our information may be as complete as possible. (The writer favors Vaughn's theory, possibly because it is more easily understood, and, for the reason that Vaughn's hypothesis will form the basis of a good portion of the subsequent discussion, it will be reserved for the last.)

As previously stated, Besredka refuses to accept any poison or poisons as the causative factors of anaphylaxis. In order that his side may be justly presented without distortion of meaning the following extract is given from Gloyne's translation of "Anaphylaxis and anti-anaphylaxis and their experimental foundations"—Besredka, 1919. "In our opinion, the anaphylactic poison does not exist. . . . . In order to presume nothing as to the nature of the antigen or its antibody, we have referred to them under the names of sensibiligen and sensibilisin. What takes place at the time of trial injection? The newly arrived antigen (horse serum or other foreign substance) comes into contact with the already formed sensibilisin. The effect of their affinity is to produce an intense reaction. Whether this reaction disturbs the equilibrium of certain nerve cells where the combination takes place, or whether the latter is accompanied by the setting free or the absorption of energy, calorific or otherwise, we have presented to us a series of phenomena always the same, and which constitute the anaphylactic shock. In adopting this term, our idea was to exclude carefully all idea of intoxication, and to indicate, on the contrary, that, in our opinion, it was simply a case of violent disturbance without the formation of a fresh chemical substance. What governs anaphylaxis and anti-anaphylaxis is neither the toxin nor the antitoxin, but on the one hand, the rate at which the sensibiligen and the sensibilisin come into contact; and, on the other, the place where they meet, which is probably the nervous system." With all due respect to this distinguished investigator who has done so much for serum therapy by developing anti-anaphylaxis his theory is altogether too vague to be satisfying.

According to Vaughn (6) anaphylaxis is caused by the absorption of the essential poison group split from the complex protein molecule incident to the cleavage or digestion of the protein by the specific proteolytic ferment elaborated by the body cells for the special purpose of simplifying and preparing the complex molecule for absorption or elimination.

Vaughn draws an analogy between the reduction of proteins in alimentary digestion and the cleavage which must occur when these substances are introduced into the parenteral circulation. In the alimentary canal proteins must first be digested before their nutritive principles can be absorbed. The large and complex protein molecules must be split into smaller, more simple molecules. "Every protein molecule contains a poisonous group, and in normal alimentary digestion this group is rendered non-poisonous by further cleavage before absorption takes place. When foreign proteins find their way into the blood and tissues they must be digested. This is accomplished, as

it is in the alimentary canal, by proteolytic ferments, but the danger from the poisonous group in the protein molecule is evidently greater in parenteral than in enteral digestion. Both enteral and parenteral digestion are physiological processes. Every living cell has its own proteolytic ferments, otherwise it could not live. When stimulated it pours out this ferment, and it does so only when stimulated. The function of a cell ferment depends upon the kind of cell elaborating it, and, to a certain extent, upon the stimulating substance. The proteins are the normal stimulants to cell secretion. When a foreign protein is introduced into the blood or tissue it stimulates certain body cells to elaborate that specific ferment which will digest that specific protein. When such a protein first comes in contact with the body cells the latter are unprepared to digest the former, but this function is gradually acquired. The protein contained in the first injection is slowly digested, and no ill effects are observable. When subsequent injections of the same protein are made, the cells, prepared by the first injection, pour out the specific ferment more promptly and the effects are determined by the rapidity with which the digestion takes place. The poisonous group in the protein molecule may be set free so rapidly and in amount sufficient to kill the animal." This, briefly, is Vaughn's explanation of the phenomena of anaphylaxis. It makes a special appeal because it is founded upon well understood physiological principles.

The animal best suited for experimental purposes is the guinea pig. The antigen or sensitizing agent which most nearly fills the requirements for an anaphylactogen is horse serum. Horse serum is, however, of greater interest than any other animal or vegetable protein for it forms the base of practically all of the prophylactic and curative sera used in the human subject.

When injected experimentally, blood serum sensitizes the laboratory animal (guinea pig) in from 10 to 12 days, whether the inoculation be subcutaneous, intravenous, intracranial, or intra-abdominal.

The amount of serum essential to sensitization is surprisingly small, in fact, small amounts sensitize more regularly and uniformly than large doses. In this connection it is interesting to note that sensitization developes more slowly in the presence or large initial doses, the incubation period being prolonged in proportion to the quantity of serum used. The reason for this is s mewhat obscure but a logical explanation may be arrived at by applying Vaughn's reasoning. The protein of the first injection is slowly digested. The larger the initial dose the longer the time required to dispose of it. Sensitization is not accomplished until the body cells accumulate a reserve of proferment and this is not possible until the excess of protein material has been used up and ferment absorption discontinued.

The avenue of entry of the sensitizing agent into the body also modifies the effect. Intravenous and intracranial injections produce the most rapid and uniform reactions while the greatest delay is experienced when intraperitoneal inoculations are resorted to.

While it is generally agreed that small initial doses of serum more rapidly produce the condition of sensitization it must not be forgotten that large amounts given at one time sensitize as well, and as certainly, if

a sufficiently prolonged incubation period be permitted before the injection of the exciting or toxic dose. The size of the second dose has a direct bearing upon the intensity and gravity of symptoms produced, the larger the dose the more immediate and dangerous the shock liable to develop. It seems that the second dose must be many times larger than the sensitizing dose in order to produce the anaphylactic phenomena but the amount required is not easily determined nor is it constantly the same. Vaughn is of the opinion, that the second dose, in order to produce symptoms of anaphylaxis, must contain sufficient protein to furnish a toxic amount of the poisonous group, and that any dose containing this amount will produce anaphylactic symptoms in sensitized animals, provided the digestive process proceeds rapidly enough to liberate toxic amounts of protein poison before further digestion eliminates the danger.

By special and original methods Vaughn and Wheeler were able to separate or at least demonstrate the presence of a poisonous group in a variety of proteins. The reasons Vaughn assigns for considering this protein poison and the anaphylactic poison identical are as follows: (a) The protein poison exists in all true proteins, so far as they have been tested, consequently it exists in all anaphylactogens: (b) Whatever the protein from which the poison is obtained its physiological action is the same. While there may be and probably are chemical differences in the protein poison as obtained from diverse proteins, physiologically there is no difference. Likewise the symptoms in anaphylaxis are the same whatever the anaphylactogen. (c) The symptoms induced in fresh animals by the protein poison are identical in every detail with those observed in sensitized animals after reinjection. They come on in the same time, proceed in the same order, and terminate alike: (d) Friedburger has shown that guinea pigs killed with the protein poison show the Auer-Lewis phenomenon in the lungs: (e) Edmunds has shown that dogs killed with the protein poison manifest the same symptoms as those studied in anaphylactic shock. The lowered blood pressure found in anaphylactic shock and in peptone poisoning in dogs is just as marked in those under the influence of the protein poison: (f) Our (Vaughn and Wheeler) poison is the active principle in peptone, and when it has been extracted from peptone the residue is no longer poisonous: (g) When the poison has been removed from an anaphylactogen the residue may or may not sensitize, but in no case does it induce the symptoms of anaphylaxis on reinjection: (h) Other reasons are cited, based upon the known facts of the digestive process, in which the products of digestion are shown to be more poisonous than the undigested substance.

Vaughn's experiments show that the non-toxic group of the protein molecule sensitizes while the poison group never does. He concludes that all proteins contain a physiologically identical poisonous group which accounts for the similarity of symptoms of anaphylactic shock, whatever the protein injected, while the non-toxic or sensitizing group is not the same in any two proteins, hence the specificity of sensitization. The exhaustive work of Vaughn, and Wells and Osborne seems to establish the fact that the specificity of the protein sensitization

reaction is determined by the chemical constitution of the protein rather than by its biological origin.

"As regards clinical manifestations the first injection of a foreign protein is without effect on the animal organism but in reality profound and long enduring changes are induced. From the time of first injection until the body is recognizably disturbed by a reinjection the incubation period or "pre-anaphylactic state" is experienced. During this period certain body cells, long dormant, are stimulated to produce the specific digestive substances necessary to break up the unwelcome invader. The wonderful biologic reserve s are mobilized and even though superficially unchanged the recipient reacts vigorously to the stimulus of the protein sensitizer. Reinjections during the incubation period of 10 to 12 days will not produce shock and will perhaps prolong the "pre-anaphylactic state." At the end of this time, however, the animal has entered the anaphylactic state and will continue hypersusceptible to reinjections of the specific protein for an indefinite period, perhaps for life.

The symptoms of anaphylaxis induced by the reinjection of a homologous or closely related protein in a sensitized animal vary within certain limits in different species of animals, but in the same species are constant, whatever the protein used. The variation in symptoms is perhaps due to the variations in organs affected, and this, according to Schultz, is based upon the distribution of smooth muscle in general. Schultz concludes from his experiments that during the anaphylactic shock all smooth muscle contracts, the degree and continuousness of this contraction determining the outcome of the shock.

The guinea pig dies of asphyxia. In the peculiar, though normal, anatomy of the bronchial tree of this animay, the mucosal layer of the secondary bronchi is relatively thick in comparison with the lumen, and the contraction of the smooth muscle throws it into folds which completely precludes the intake of air. (Observations of Schultz and Jordan-Rosenau's Preventive Medicine and Hygiene.)

The bronchi of mice, dogs, and rabbits, however, are relatively poor in smooth muscle, which accounts for the almost complete absence of death from asphyxia. In the dog the contraction of smooth muscle sets up a vigorous intestinal peristalsis and a forced emptying of the urinary bladder. The characteristic rise in blood pressure may be due to contraction of the pulmonary, coronary, and systemic arteries, and, according to Auer, the subsequent marked fall is occasioned by direct action of the protein poison on the heart muscle, the right side being particularly affected, with consequent venous accummulation of blood. This phenomenon is especially well demonstrated in the rabbit. The reasoning of Schultz and Jordan provides an adequate pharmacological explanation for the action of atropine and anesthetics in alleviating the symptoms of acute anaphylaxis.

Three stages of the anaphylactic reaction are recognized. In experimental production it is necessary that the process be permitted to develop slowly fo rthis reason the reinjection is given intraperitoneally (Vaughn-Protein Split Products 1913).

The first stage is that of **peripheral irritation.** The animal is excited and evidently itches intensely, as is evidenced by its attempts to scratch every part of the body it can reach with the feet.

The second stage is that of **partial**

paralysis. The animal lies on its side or belly, with rapid, shallow and difficult breathing. It is disinclined to move, and when urged to do so shows more or less inco-ordination of movement, and muscular weakness, with partial paralysis, especially observable in the posterior extremities, which it drags. The animal rarely dies in this stage.

The third or **convulsive stage,** begins with throwing the head back at short intervals. The convulsions become general, more frequent and violent, and the animal having reached this stage, usually dies in a convulsion or immediately following one. Expulsion of urine and feces is frequent in this stage. Animals reaching the third stage of anaphylactic shock rarely recover. On the other hand less severe reactions are followed by recovery, so promptly and completely, that in a few hours generally the animal cannot be distinguished from perfectly healthy controls.

The picture of characteristic anaphylactic shock is an exact reproduction of the condition caused by the injection of the protein poison isolated by the method of Vaughn and Wheeler and seems to positively confirm the hypothesis advanced by the former regarding the bio-chemistry of the manner of production.

When the homologous protein is injected into a man sensitized by disease or previous treatment, symptoms develop promptly, often within a few minutes, usually within a few hours. The stage of peripheral irritation is characterized by the sudden appearance of a rash. Rashes occurring most commonly and promptly are urticarial and erythematous. The lips and tongue seem swollen, and the backs of the hands and feet are swollen. The individual becomes apprehensive, feels that he cannot breathe, and falls into a state of more or less marked collopse. In extreme instance sthere is retching and vomiting. The second stage, that of great muscular weakness, continues for a variable time and usually passes away rapidly. In rare instances speedy death results.

One of the most easily recognizable and constant features in anaphylactic shock is fall in blood pressure. The work of Biedle and Kraus (1910) explains the production of this fall. There is a complete parallelism between the clinical symptoms and the fall in blood pressure. As the latter proceeds the former increases in intensity, and in recovery the rise accompanies the return to normal. Irrespective of the stage of pressure or other symptoms the corneal and cutaneous reflexes remain intact throughout and exclude a central narcosis or peripheral muscular paralysis.

The genesis of the fall in blood pressure is most interesting and as outlined by Biedle and Kraus (1910) is reviewed by Vaughn as follows:

"The type of fall and the accompanying condition of the pulse rules out weakness of heart action. It is generally accepted that a fall in blood pressure accompanied by increased frequency of the pulse rate is not due to decreased strength on the part of the heart but is most probably a result of decreased peripheral resistance. The decreased peripheral resistance with consequent fall in blood pressure is accounted for by marked peripheral vasodilation. Such vasodilation may be due either to paralysis of the vasomotor center or to action on the peripheral structures. Experimental work shows conclusively that the vasodilation of anaphylactic shock is due to a transitory paralysis

of the peripheral vasomotor apparatus. The effect of barium chloride in overcoming the fall in blood pressure while adrenalin chloride fails renders it highly probable that the anaphylactic poison lowers blood pressure by paralysis of the smooth muscle of the vessel walls."

"Having established the fact that fall in blood pressure is a marked and constant result of the anaphylactic poison, the symptoms become easily explainable. The resulting anemia of the brain explains the disturbances of respiration, the retching, the expulsion of urin and feces, the great depression and muscular weakness, and the speedy recovery, when death does not result."

Two types of anaphylaxis are recognized. We have considered active anaphylaxis, in which the animal is sensitized, and subsequently shocked by the reinjection of a homologous protein. Passive anaphylaxis is induced when the blood serum of a sensitized animal is introduced into a fresh animal, which may be of the same or another species. The transfer of the condition of sensitization from mother to offspring is an example of homologous passive anaphylaxis. A fundamental difference between active and passive anaphylaxis is that no incubation period is required for the production of the latter.

The relationship between anaphylaxis and infection is clearly set forth by Vaughn in a special chapter devoted to this phase of the study, and is both plausible and convincingly developed.

An infecting virus may be solid, semisolid, gelatinous, or liquid. Bacteria represent the solid or particular type of infecting agent. To thoroughly understand Vaughn's reasoning it is necessary that we consider bacteria as highly developed protein bodies, of complex chemical structure, possessing the attributes characteristic of other living matter—the capability of growth and reproduction. "In order to grow and reproduce the molecular structure of the organism must be in a state of constant change. This activity consists of the constant interchange of matter between the bacterium and the medium in which it exists. In order for the nutrient material of the medium to be used as food it must be made to fit into the molecular structure of the feeding bacterial cell. Many kinds of cells may live in the same or like medium, but for each kind of cell the requisite food must be prepared by molecular cleavage, the specificity of which is dictated by the structure of the cell to be fed. It follows that the agent by which the cleavage products are secured must be supplied by the cell itself. These agents, whose function it is to prepare food for the cell, are known as ferments. If the ferment elaborated by a given cell is ineffective against the medium in which the bacterium is placed food cannot be secured and the cell dies. The ferments produced by the majority of bacteria cannot digest and break up the protein of the animal body and they for this reason are recognized as non-pathegenic or harmless bacteria."

"What is true of bacterial cells is equally true of the fixed or movable body cells. These cells properly stimulated produce ferments or cleavage agents and the bacteria being protein substance may be digested by the ferments elaborated by the body cells. In the inability of the baeterial cell to grow in the animal body, either because it cannot feed upon the proteins of the body, or because it is itself destroyed by the ferments elaborated by

the body cells lies the fundamental explanation of all forms of immunity to bacteria, either natural or acquired."

In the instance of bacteria producing specific poisons or toxins, the toxins act as ferments and lead to the production of anti-ferments, or antitoxins. The diphtheria bacillus is one of the best known organism of this type and according to Vaughn, acts as follows:

"Having found lodgment and a favorable environment in the upper air passages, this organism grows prolifically. It produces a soluble, diffusible toxin which has the properties of a ferment and splits up the proteins of the body, setting free the protein poison. If the body cell elaborates a sufficient amount of antiferment or antitoxin the toxin or active ferment is neutralized and protein cleavage is prevented." Vaughn is of the opinion that death in diphtheria is not due to the direct action of the diphtheria toxin but to the poisonous group of body proteins split off by toxin-ferment action.

"Cell ferments are of two classes. Extra-cellular ferments which are strictly lytic bodies, breaking up protein substances into simpler substances, and intra-cellular ferments which take the simplified substances brought to the cells and further shape them for fitting into the molecular structure of the body cell. In the case of an infectious disease the intracellular ferment of the infecting organism during the period of incubation converts man's protein into bacterial proteins, and continues to do so throughout the disease. In some diseases this is accomplished without any marked disruption of the body cells and it follows that the body proteins are converted into bacterial proteins without the liberation of the poisonous group. This conversion of protein material, however harmless during the incubation period, is not accomplished without sensitizing the body cells, and these quickly learn to elaborate a special ferment which breaks down the bacterial cells, the poisonous group in the proteins of the latter is set free, and it is the effect of this poison that develops the symptom-complex of the disease."

"The clinical manifestations of anaphylaxis are determined by the rapidity with which the protein poison group is liberated and also by the amount of toxic material to which the body cells are exposed. When the poison group is liberated with explosive rapidity and in large amount it induces anaphylactic shock, and perhaps death. When set free slowly and in small amount, either fever or a fall in temperature are noted, according to the amount of poison liberated. When set free either in the circulating fluid or when it passes in to this fluid immediately systemic effects are produced, or when set free locally inflammatory reactions in adjacent tissue are produced." (Vaughn.)

"As ordinarily used the term anaphylaxis refers to the symptoms of anaphylatic shock. In a wider sense it covers all of the phenomena of parenteral protein digestion." While the majority of observers consider parenteral digestion abnormal Vaughn does not agree and advances certain facts in proof of his contention. "By inhalation, through abrasions, and possibly through the alimentary canal, man must be frequently, almost constantly, taking into his blood and tissues very minute traces of undigested proteins, but ordinarily the amounts thus taken are so infinitesimally small that the body cells are not sensitized, and no harm comes. While, as we

have seen, some anaphylactogens sensitize in very small doses, these are not infinitesimal, and there are measurable doses which do not sensitize. The limits vary with the protein and the animal." (Vaughn.)

We now come to the essentially practical considerations of the clinical manifestations of "serum sickness" or other phenomena occurring during the administration of sera or other foreign protein substances as prophylactics or curative agents.

The identifying name "Serum Sickness" was applied by Von Pirquet and Schick (1905) to the various clinical manifestations, such as eruptions, fever, oedema, and pain in the joints, following the injections of horse serum. These symptoms were due to the horse serum itself, and were not related to the antitoxin content of sera as was early shown by Johannessan (1895) and Bokay (1897), who produced identical symptoms by the injection of sterile normal horse serum.

The serum of certain horses appears to be more likely to produce these symptoms than that of others, and this accounts for the fact that one lot of antitoxin will cause a higher percentage of serum sickness than another. A concentrated serum is less likely to cause unfavorable sequelae than whole serum, owing partly to the fact that less protein material is contained in the smaller dose. According to Rolleston and Ker, the frequency of serum sickness is, as a rule, in direct proportion to the amount of serum given, and in inverse ratio to the severity of the attack; in other words, we may expect to encounter it most often in mild and moderately severe cases of infection that have received very liberal dosages of serum.

There is no longer any doubt as to the nature of this condition. Serum sickness is a true anaphylactic phenomenon. The medical profession has accustomed itself to distinguish between the severe and often fatal reaction of acute anaphylactic shock, and the relatively moderate reactions collectively distinguished as "serum sickness", and so have lost sight of the fundamental relationship. Both are examples of anaphylaxis and differ only in time of appearance and in severity of symptoms. In the instance of acute anaphylactic shock the body cells are for some reason unduly and highly sensitive, occasioned no doubt by having been previously grossly stimulated to the production of proteolytic ferments. The history of these cases will invariably show that the subject has either been injected at some time or other with homologous protein material, or is of the hypersensitive or asthmatic type, in whom there persists a constant hypersensibility to emanations from horses.

While serum sickness is usually due to horse serum, for the reason that the horse is so commonly employed in the preparation of various curative sera, the serum of the ox, rabbit, and other animals may induce the same train of symptoms, in addition, in some instances, to producing a direct toxic effect.

An immediate reaction rarely follows the first injection of serum except in the instance of persons who have in some manner been rendered hypersensitive to the protein injected. In the majority of instances symptoms do not develop for from 8 to 12 days, during which time the body cells are producing the special substance capable of splittin gthe foreign protein. When this protective production has reached a certain point,

the antibody or ferment reacts upon the excess protein material remaining in the cells or circulation, cleaving the complex molecules and liberating the poison group which exerts its specific toxic effect with the production of moderate anaphylactic shock or serum sickness.

If a small amount of protein has been introduced, as is the case when using highly concentrated antitoxins, an insufficient amount of poison may be liberated and the subject escapes an unusual reaction. This is usually the case, it appears, as ordinarily first injections are not followed by anaphylactic manifestations, but we must understand that the process of sensitization goes on just the same and even the fortunate individual who first escapes through lack of sensitiveness is now sensitized, and, if subsequently reinjected, is liable to the rapid production of acute shock if this serious contingency is not guarded against.

The symptoms of serum sickness may be found in any number of texts and will be considered here in only a general way.

The most obvious and important of the symptoms are undoubtedly the various forms of rash. The three main types of rashes generally recognized are: () Prticarial, usually after the seventh day, becoming manifest first about the site of injection. True urticaria and rashes of urticarial type constitute from 70 to 90% of all eruptions. (2) Multiform rashes—This type is quite common. Different parts of the body may present totally different appearances at the same time. This rash may occasionally simulate trué measles, especially since it involves the face, and as the conjunctiva are likely to be congested in any variety of serum sickness. Absence of Koplik's spots, absence of prodromal rise of temperature, and the fact that the eruption most frequently starts from the site of injectio ninstead of on the face, serves to differentiate this rash from measles. (3) Scarlatiniform Rashes — This type only occasionally occurs but must be differentiated from scarlet fever. The rash usually appears from 1 to 6 days after injection to a true punctate scarlatinal rash. Absence of high fever, typically furred tongue, angina and leukocytic inclusion bodies rule out scarlet fever.

In addition to the three types of rashes ordinarily encountered the most typical symptoms met with in serum sickness are, fever, and prostration, besides joint and muscle pains, oedema, and adenitis.

Sever forms of serum sickness, followed by death, are rare but are not impossible of production, and the physician may not escape the responsibility of causation if he has failed to eliminate certain conditions absolutely contraindicating the administration of horse serum. Horse serum must not be administered in status lymphaticus or to to individuals known to be hypersensitive to horse serum. Persons suffering with asthma are bad risks, especially since the effects of serum disease upon the bronchial mucosa are likely to aggravate the already existing condition.

In this connection it may be well to state, that in the great majority of cases, the administration of a cerefully prepared and properly administered serum is free from danger, provided obvious cases of hypersensitiveness be altogether excluded. If there is a well defined need of prophylactic or curative administrations the practitioner should not hesitate to take advantage of the great benefits derived from the early administration of the specific so

readily obtained. The exercise of proper discrimination and care on the part of the physician will obviate the very real dangers of the production of anaphylaxis, secure early and correct treatment for the sufferer, protect the valuable procedure of specific serum therapy from adverse criticism, and, finally, relieve the State from the great and unnecessary expense incident to the purchasing of large amounts of serum to be wasted by indiscriminate and useless administration.

The anaphylactic phenomena have been practically applied, in fact, since long before the identity was recognized . In the instance of vaccinia, the reaction to a primary "take" appears after an incubation period of about 4 days. In a secondary vaccination the period of incubation is considerably shortened and the clinical reaction lessened. The immunity conferred by vaccination against small-pox is due entirely to the anaphylactic state in which the individual remains after sensitization to the specific protein in the virus.

The tuberculin reaction in persons suffering with tuberculosis, and the mallein reaction in the presence of an infection with glanders are each instances of hypersusceptibility to a homologous protein.

Clinical examples of protein supersusceptibility are found in hay fever pollen sensitization, epidermal asthma, and food idiosyncracies. The latter phenomenon is commonly met with and is familiar to most of us in a strictly personal use.

The sensitiveness which some individuals possess wit hregard to protein articles of diet would appear to be explainable on the ground that, through some abnormal condition of the intestinal mucosa, certain protein substances are allowed to enter the body in an unchanged condition. The symptoms which appear are strikingly suggestive of those described in connection with protein sensitization accomplished by direct injection. The mechanism of the sensitization by the intestinal route is in a general way identical with that already described. Once theunchanged protein enters the parenteral circulation the body cells are called upon to elaborate a specific proteolytic ferment to counteract the abnormal condition thus produced. The excess ferment is stored up in the cells as a zymogen for future use. Protein substances subsequently entering the parenteral circulation are subjected to the same splitting ordinarily performed in the intestine but the poison group is liberated directly into the body itself and consequently exert immediate harmful influence. It not infrequently happens that hypersusceptible persons ingest quantities of the protein to which they are sensitive without anaphylactic reactions and this is explained by the fact that by reason of previous indulgence the excess zymogen has been exhausted and the body cells have not had time in which to elaborate a new supply.

For the past few years there has been an icreasing tendency on the part of the public to demand, and on the part of the practictioners of medicine to prescribe specific treatments for all manner of ills.

This has lead to the production and xploitation of numerous sera, prophylactic and curative, to say nothing of the large and ever increasing list of vaccines, bacterins, phylacogens, etc. This tendency betrays an increasing interest in the more scientific application of the practice of medicine, but unless carefully and conservatively curbed will lead many earnest workers

into error, and by reason of the increase of the number of unfavorable reactions following the administration of such specifics will no doubt direct harmful criticism to a procedure, which may well be considered the ultimate in therapy.

We must immediately arrive at the proper understanding of the fundamental facts in the case. All bacterial and serum preparations are basically of protein substance. Protein substances are of complex molecular structure, the molecule of which contains both toxic and nontoxic groups. We cannot introduce such substances into the human economy without setting up reactions which may be either helpful or harmful, depending upon the careful selection of case, treatment and proper dosage of the correct preparation, or the indiscriminate use of "vaccines" of divers origin and composition. When there have been produced protein substances from which the poison group has been entirely removed, then, and only then, will serum therapy be fool-proof, and the every day administration of such specficis lose its potential danger.

Specific instances of the danger referred to are found in the protein sensitization which may result from the administration of prophylactic doses of diphtheria and testanus antitoxins. that the danger of inducing the condition of protein hypersusceptibility is much greater when using the serum preparations than bacterial suspensions is manifest and easily understood as the sera invariably contains a vastly greater amount of protein substance which is usually sufficient in amount to stimulate the production of sensitization, and to provide for an excess of the proferment which persists in the body cells over an indefinite period of time. That the use of immunizing doses of tetanus antitoxin in cases of known exposure, such as penetrating wounds of areas of the body exposed to dirt or stable contamination is justified is unquestioned for the condition we seek to prevent is more terrible than the probability of acute anaphylactic shock. In the instance of immunization to diphtheria, however, the introduction of a large amount of protein substance is attended with so little benefit as compared to the grave danger of the production of a fatal anaphylactic shock, should it ever become necessary to inject either diptheria or any other antitoxin, that the procedure is subject to serious criticism.

A critic who criticises without offering practical suggestions for correction, or a physician who diagnoses without presenting a remedy could not be either successful or popular. The major portion of this paper has been utilized in building up a case against anaphylaxis so it is only fair to the reader who has waded through to this point to devote some time to the consideration of corrective measures.

We have shown that the normal individual who has received one injection of foreign protein into the parenteral circulation has become sensitized to reinjections of the same substance. Should it ever become necessary to administer an anti-toxin or other therapeutic agent, the body of which was composed of the same protein, the sensitized individual would certainly be exposed to all of the dangers of anaphylactic shock. We believe that if the procedure devised by Besredka be carefully followed these sensitized persons can be "desensitized," or temporarily returned to the normal, so that the necessary serum therapy can be undertaken without danger. The wonderful benefits of this simple method must become apparent to all

who have followed the preceeding discussion. The terms "Anti-anaphylaxis" and desensitization are used interchangeably.

The term anti-phylaxis was first applied by Besredka and Steinhardt to a condition of insensibility to further injection of the anaphylactogen that may follow recovery from anaphylaxis or be induced artificially bya single or by repeated small injections of the anaphylactogen during the period of incubation following the first injection, and before sensitization is complete. The state is usually only temporary, the animal gradually becoming sensitive again after three weeks.

It has long been known that the larger the first or sensitizing dose of antigen (foreign protein), the greater must be the dose of the second or intoxicating injection to cause anaphylactic symptoms. This indicates that a large sensitizing dose introduces the factor tending to produce the condition of anti-anaphylaxis. Partial desensitization, or anti-anaphylaxis, may be produced by the injection of a sublethal intoxicating dose during the period of incubation or at its close.

Besredka and Steinhardt observed that the refractory state could easily be developed in sensitized guinea pigs by one of the following methods: (1) The intra-cerebral injection of 0.25 C. C. of horse serum before the expiration of the period of incubation (12 days.) (2) The intracerebral injection of less than the fatal dose after the period of incubation. (3) Rectal injections of from 5 to 10 C. C. of serum. (4) By slowly reinjecting small amounts of horse serum while the animal was deeply anesthetized (Rosenau and Anderson subsequently showed that a narcotic might mask but did not prevent the occurrence of severe and fatal symptoms.) Of the methods described Besredka prefers the subcutaneous or intavenous injection of less than the fatal dose.

The mechanism of anti-anaphylaxis is not clear, even the name applied to the phenomenon is seemingly incorrect. The animal is not entirely and permanently anti-anaphylactic, but subsequently again becomes sensitive. The blood serum of refractory or anti-anaphylactic animals does not confer a similar condition on a second sensitized animal.

From the mass of experimental work done two factors in the production of anti-anaphylaxis have been developed. There is possibly a true "desensitization" depending upon the absorption of excess proferment by repeated small doses of antigen, and in addition, of secondary importance, is the possible development of tolerance by the body cells for the anaphylactic poison.

Regardless of the method of production, the refractory state is of the greatest importance in the handling of sensitized persons to whom sera must be administered, and the various procedures suggested are worthy of consideration. Even if it were possible to discontinue the use of prophylactic injections of protein material there would still remain a large number of human beings, both adult and young, who have already become sensitized. These will perhaps remain susceptible to anaphylactic shock for an indefinite period and if possible they must be protected from the unfavorable consequences which may be expected from a reinjection of horse serum.

Of all the methods advocated for the production of the protective condition of anti-anaphylaxis or dessensitization that of Besredka (Anaphylaxis and Anti-anaphylaxis-1919) is the most scientifically developed and productive of the most constant results as applied

to the experimental animals. Besredka vaccinates against anaphylaxis by administering numerous small doses of the homologous serum over a short period, gradually increasing the amount given until the subject is protected against many times the lethal dose of poison.

(From this point on Glyone's translation of Besredka's monograph "Anaphylaxis and Anti-anaphylaxis"-1919, is quoted almost verbatim.)

Irrespective of the route chosen, subcutaneous, intrathecal, or intravenous vaccinations serve to protect the animal against anaphylaxis. The route to be selected for vaccination shall be dictated solely by the state of the patient, and by the necessity for more or less rapid intervention. The most rapid vaccination route is the intravenous, complete anaphylactic immunity being produced in from ten to fifteen minutes.

Besredka is of the opinion that it is well for the attending physician to be informed of the patient's past serum history, but advises against placing too much reliance upon statements made either by subject or family. In this connection it must not be forgotten that there are individuals, who, without having had a previous injection of serum, react to the first injection in a violent manner. As a means of obviation all possibilities of unfavorable reaction the subject who is about to receive an injection of serum should be tested for hypersensitiveness. A test injection of a very small amount of the serum to be injected should be given to all cases, but especially to those to be subjected to intravenous or inthrathecal inoculations.

Of the most serious serum mishaps are those associated with the administration of curative serum to patients attacked with cerebro-spinal meningitis. Frequently the grave condition of the sufferer demands immediate treatment, which consists of the introduction of a large amount of foreign protein (horse serum) directly into the spinal cavity, or intravenously, thus increasing the danger of sever anaphylactic shock.

Adequate protection is afforded the meningitis patient, sensitized by the disease or by previous injection, by the procedure of Besredka.

If the condition of the patient permits delayed use of the serum while waiting for laboratory confirmation of diagnosis, it is well to take advantage of the opportunity to inject 10 to 20 c. c. of the serum subcutaneously. This preliminary injection will in no wise benefit the meningitis if present, but will most certainly tend to immunize the subject against anaphylactic shock if it become necessary to introduce serum into the spinal column.

If there is no doubt about the diagnosis, as may be the case in the midst of a recognized epidemic of cerebrospinal meningitis, the immediate use of curative serum is indicated. In this instance even the most urgent case will permit of some delay, certainly until anaphylactic prophylaxis can be practiced. Two procedures are offered, the choice between the two to be determined by the gravity of the patient's condition.

If a reasonable delay will not militate against the patient's chances for recovery give an intra-spinal injection of 2 c. c. of serum; wait one or two hours to elapse, then reinject the same route a full dose of from 20 to 30 cubic centimeters.

If no delay can be countenanced carry out the anti-anaphylactic vaccination intravenously. Begin by diluting the serum (5 c. c.) in 6 times its volume physiological saline solution;

inject 1 c. c. of this solution intravenously at the bend of the elbow. If the patient does not react within 5 minutes inject 3 c. c. of the same solution. If no untoward symptoms appear in 2 minutes longer inject 10 c. c., wait 2 minutes more and inject finally 25 c. c. of solution. "From this time on the patient may be regarded as vaccinated against anaphylactic mishaps."

Besredka's experience with a large number of cases leads him to state that within 10 minutes after completing the vaccination the patient is in a position to tolerate an intravenous or intsathecal injection of 10 to 30 c. c. of undiluted serum.

Information experimentally gained shows that anti-anaphylactic vaccination is produced:

(a) In 3 to 4 hours subcutaneously.

(b) In 1 to 2 hours by intraspinal injection.

(c) In 10 to 15 minutes intravenously.

Anti-anaphylaxis can unquestionably be produced by the oral administration of the protein substance but it is the least practical of all methods as it requires at least one or two days before immunity is established.

For human subjects only the subcutaneous, intrathecal, and intravenous routes are recommended, and the choice can only be determined by the requirements of the case in hand.

The intravenous route is under all circumstances the method of choice because it is rapid, and certain, and protects against skin anaphylaxis as well as general shock. As soon as immunity is established, which requires not more than 15 minutes, a strong dose of serum can be injected equally well intrathecally, intravenously, or subcutaneously, without the patient running the least danger of anaphylaxis. The intravenous method has the additional advantage, that one may observe, with the needle still in the vein, the sensitiveness of the patient. Begin by testing sensitiveness by introducing (intravenously) a very weak dose of 0.1 c. c. of serum. (Serum dilution is accomplished by mixing 1 c. c. of serum with 10 times its volume of physiological saline solution—1 c. c of the dilution representing 0.1 c. c. of serum.) If the patient does not react at the end of from 3 to 5 minutes 0.3 c. c. of serum (3 c. c. of dilution) is injected without withdrawing the cannula. Again wait 2 minutes and if nothing happens inject 1 c. c. of serum (10 c. c. of dilution.) It is believed that anaphylactic immunity has by this time been acquired but for more perfect security, after a further interval of 2 minutes, a last injection of 2.5 c. c. of serum (25 c. c. of dilution is made. A patient so treated will safely tolerate 20 to 40 c. c. of undiluted serum at any stage of the illness.

Anaphylactic immunity must not be confused with anti-toxic or anti-bacterial immunity. These three are related only that they possess the common attribute of specificity. Ordinary antitoxic and anti-bacterial immunity is not established until after the lapse of at least 8 days, becomes more effective as the number of injections is increased, and is more permanent than anaphylactic immunity. Anti-anaphylactic immunity is established instantaneously, is not accompanied by the appearance of antibody, but, on the other hand, by the disappearance of that substance which produces protein hypersensitiveness. Besredka considers anti-anaphylaxis as strictly a desensitization in which body cells return to their normal state. This conception seems to be bourneout as the desensitized animal may again be ren-

dered hypersensitive by the injection of protein material.

Besredka's views may be summed up as follows:

Every normal individual is anti- anaphylactic. Unless sensitized first injections of protein material are without harmful effect.

The injection of foreign protein results in the production of a substance sensibilism, a specific antibody to the protein injected.

So long as uncombined sensibilism circulates in the body the subject is hypersensitive to the reinjection of the antigen or protein material which stimulated its production.

Anti-anaphylaxis (a normal state), or desensitization, is accomplished by neutralization of sensibilisin.

By the injection of a series of graduated small doses of antigen (horse serum usually) the sum total of sensibilisin is neutralized resulting in the complete desensitization of the subject.

To accomplish the desired result it is necessary to inject the maximum dose of antigen campatable with the non-production of anaphylactic symptoms.

To be in a position to know when the optimum dose of antigen has been administered, and anti-anaphylactic advises to proceed with the injection immunity has been acquired Besredka of antigen until the "precritical" dose has been reached. The effect of this dose is shown in man by the appearance of anxiety and a redness of the face lasting some minutes. These manifestations are absolute proof that desensitization has been accomplished and that the patient will tolerate any amount of serum necessary for therapeutic purposes.

Besredka urges that the physician should assume the attitude that all individuals to whom large amounts of serum are to be administered are hypersensitive. In this connection he advises one to always commence with weak doses, proceed rapidly without stopping if no reaction occurs during the intervals recommended, and to go on injecting stronger and stronger doses until the precritical dose is attained. If this precautionary routine is strictly adhered to serious serum "accidents" will be avoided.

The direct relationship between the condition of hypersensitiveness and all forms of immunity is becoming more and more apparent all the time. The opinion has been expressed that resistance to disease may largely be gained through sensitization. Whether the increased susceptibility is an essential element, or only one stage in the process of resistance to disease, is not yet determined but there remains no question but that the specific reactions of body cells to protein substances has an important bearing on the prevention and cure of infectious processes.

Sensitization occurring as a result of the entrance of bacterial cells into the body represents a beneficial process. Since, under ordinary conditions, pathogenic bacteria represent the only proteins which gain entrance to the body in an unchanged condition, one may reasonably conclude with Vaughn that sensitization or protein hypersusceptibility arises as an attempt of nature to combat bacterial invasion.

This great force may some day be directed so scientifically for the protection of diseased individuals, and under such complete control of the manipulator, that the phenomenon of sensitization may be customarily utilized in the prophylaxis and treatment of infectious processes due to

viruses of protein structure. One may reasonably conclude that protein sensitization is a manifestation of the most conservative and protective of all body forces.

BIBLIOGRAPHY

Direct references:

(1) Ch. Richet, "L'anaphylaxie", p. 3; ed F. Alcan.

(2) Comptes rend. Soc. de Biol., 1903, lv., p. 817.

(3) "Das Theobald Smithsche Phaenomen der Serum-Uberempfindlichkeit", Berlin, 1906, i., 153-172.

(4) "A study of the Cause of Sudden Death following the injection of Horse Serum", Bulletin Hygienis Laboratory No. 29, April, 1906.

(5) "De l'anaphylaxie et de l'anti-anaphylaxie, vis-a-vis du serum de cheval", Annales de l'Institut Pasteur, xxi, p. 117. "Du mecanisme de l'anti-anaphylaxie", ibid., 1907, xxi. p. 384.

(6) Vaughn "Protein Split Products in Relation to Immunity and Disease"—p. 218—Lea & Febiger, 1913.

The data collected in this article taken from:

Besredka-Gloyne—Anaphylaxis and Anti-anaphylaxis, 1919—Mosby.

Vaughn—Protein Split Products in Relation to Immunity and Disease, 1913—Lea & Febiger.

Kolmer—Infection, Immunity, and Specific Therapy, 1917—Saunders.

Zinsser—Infection and Resistance, 1918—Macmillan.

Hiss & Zinsser—A Text Book of Bacteriology, 1918—Appleton.

Rosenau—Preventive Medicine & Hygiene, 1918—Appleton.

ANNUAL REPORT OF THE STATE HEALTH OFFICER

By James A. Hayne, M. D., Columbia, S. C.

Continued from January Issue

Laboratory.

Dr. Coward's excellent report of the work of this Department will be found elsewhere in this volume. It shows that the work has increased one hundred per cent. This is due, to a large extent, to the number of Wassermann tests for syphilis. The Laboratory made twenty-seven thousand of these tests as required by Act of the General Assembly. We regard the Laboratory as perhaps the most important division of th eState Department of Health, and onethat is rendering a most valuable service. The personnel of the Laboratory is too small for the amount of work required, and the salaries are in inadequate. It requires yearsof experience an dexpensive technical education to make a bacteriologist, and we are paying only the wages of a day laborer.

We again urge the Legislature to take heed to the danger of allowing the running at large of dogs, which, when they go mad, bite individuals, causing inconvenience, suffering, and sometimes death. We have treated three hundred and eigh tpeople bitten by rabid animals this year.

The Laboratory sent out twenty-eight thousand ampules for the prevention of typhoid fever, thus immunizing nine thousand three hundred thirty-three people. The history of the World War shows that this is the most effective means of controlling typhoid fever.

Department of Rural Sanitation.

Excellent results have been obtained in the six counties in which this work has been done during 1919. The counties, through their representatives,

have expressed themselves as being very much pleased with the work done.

The International Health Board has appropriated $18,000.00 for this work in South Carolina, and the Legislature has been asked for a like amount. The counties will each be asked for $5,000.-00 to supplement. The work will be done in six counties; and as we now have a trained personnel the work should be more efficiently done this year than ever before. This rural sanitation education leads upto a county health department, which should be in each county, and the need of such an organization requires no argument. The rural population needs safeguarding as much as, if not more than, the urban, and yet there is no organization in the counties that is responsible for this work. Census reports show that, although the country has more reasons for being healthy than the city, yet the country child is not as robust as the city child. As South Carolina is a rural state we must remedy this condition, or we are not doing our full duty to the child.

Dr. L. A. Riser has charge of this Department, and his report is found elsewhere in this volume.

BOOK REVIEW

THE
MEDICAL CLINICS
OF
NORTH AMERICA
SEPTEMBER, 1919
Published Bi-Monthly by
W. B. SAUNDERS COMPANY

Among the excellent rticles in this number are the following:

Page

CUINIC OF DR. WARFIELD T. LONGCOPE, Presbyterian Hospital Cerebral and Spinal Manifestations of Purpura Haemorrhagica..... 279

CLINIC OF DR. G. R. PISEK, Post-Graduate Hospital Common Disorders of Childhood 341

CONTRIBUTION by DRS. W. W. Herrick (New York), Formerly Major M. C., U. S. A., and A. M. DANNENBERG (Philadelphia), Formerly Captain, M. C., U. S. A., Recurring Meningococcic Meningitis 379

CLINIC OF DR. ARTHUR P. GRACE, Post-Graduate Hospital and Medical School. The value of Chemical Blood Examinations in Diagnosis, Prognosis and Oreatment of Some Constitutional Conditions 389

CLINIC OF DR. GEORGE STUART WILLIS, Post-Graduate Hospital and Medical School. Radium Therapy 401

CLINIC of DR. MORRIS H. KAHN, Mt. Sinai Hospital. The Functional Diagnois of the Heart..... 433

CLINIC of DR. I. W. HELD, Beth Israel Hospital. A Discussion on the Splenomegalies 519

THE SURGICAL CLINICS OF CHICAGO
Volume III, Number 6 (December, 1919)
The Surgical Clinics of Chicago. Volume III. Number 6 (December, 1919). Octavo of 215 pages, 63 illustrations and complete index to volume 3. Philadelphia and London:
W. B. Saunders Company, 1919. Published Bi-Monthly: Price per year: Paper $10.00; Cloth $14.00.
W. B. SAUNDERS COMPANY
Philadelphia London

Among the excellent articles in this number are the following:

Page

CLINIC of DR. ARTHUR DEAN BEVan, Presbyterian Hospital, Chronic Lung Abscess with Fistula-Treatment by Excision 1317

X-Ray Diagnosis of Gall-Stones...1325

Fibrone of Large Intestine 1333

CLINIC OF DRS. DANIEL N. EISENDRATH AND MAURICE L. GOODKIND, Michael Reese Hospital. Subacute Pancreatitis (Pancreatic Abscess) 1367

CLINIC OF DR. KARL BECK, North Chicago Hospital. Old Sinus from Hip Disease Treated by Skin Sliding 1403

Diverticulum of Urinary Bladder in an Inguinal Hernia 1407

Gangrenous Hernis of the Bladder and Intestine 1411

CLINIC OF DR. COLDER McWHORTER, Presbyterian Hospital Osteomyelitis with Variarion in Growth of the Femur Following Separation of the Distal Epiphysis 1449

CLINIC OF DR. WILLIAM OHOMAS HARSHA, Illinois Central Hospitial Acromegaly 1469

CLINIC OF DR. EDWARD LOUIS MOORHEAD, Mercy Hospital. Multiple Uterine Fibroids: Secondary Anema, Nephritis 1481
Epigastric Hernia—Hernia of the Linea Alba 1485
Gunshot Wound of the Buttock ..1491
CLINIC OF DR. HERMAN L. KRETSCHMER, Presbyterian Hospital. Diagnosis of Ureteral Calculi 1503

M. D., Samuel D. Gross, Professor of
MODERN SURGERY: GENERAL AND OPERATIVE. By J. Chalmers DaCosta,

---

Surgery, Jefferson Medical College. Philadelphia, Pa. Eighth Edition, Revised, Enlarged and Reset. Octavo of 1,697 pages, with 1,177 illustrations, some of them in colors. Philadelphia and London, 1919. Cloth, $8.00 net.

W. B. SAUNDERS COMPANY
Philadelphia London

This is, perhaps, the most popular textbook on surgery in use by students and practitioners, as well, in print. The revision, while perhaps not as thorough as might have been done in normal times; yet there is much that is new and worth while.

The section on Transfusion of Blood has bee nbrought up to date. The section on Bronchoscopy and Esophagoscopy has been written by that master, Dr. Chevalier Jackson. Other contributors are Dr. S. Mac Cuen Smith. Dr. William S. Wadsworth on Electrical Injuries. Dr. George E. Pfahler, the eminent Roentgenologist. Dr. B. A. Thomas, the section on Venereal Diseases. The book now contains 1,697 pages, and is very close to the border line in which it should be published in two volumes, instead of one.

WANTED

Intelligent, Ambitious Young Women to Enter The Nursing Profession.

The Greenville City Hospital offers a course of training to young women fitting them for the field of general nursing and meeting the requirements of the Army and Navy Nursing Corps, and the Red Cross.

Pupils will be lodged in the delightful nurses home—have an eight hour working day—Daily classes or lectures.

FOR SALE

One "American Sterilizer" equipped with electric heating apparatus. Consists of one utensil sterilizer, instrument sterilizer, hot water tank, distilled water tank, and one large dressing sterilizer. New and in perfect working condition. Reason for selling leaving the State.

R. T. Ferguson, M. D.,

Gaffney, S. C.